risk of leukemia. Clinically useful alkylating agents such as cyclophosphamide and melphalan seem to produce acute myelomonocytic leukemia in some of the long-term multiple myeloma survivors. Radioactive phosphorus given for polycythemia vera also increases the risk from acute leukemia. Treatment of patients with oxymethalone or methyltestosterone derivatives has produced hepatocellular carcinoma. Diethylstilbestrol given over long periods for gonadal dysgenesis appears to sometimes result in endometrial carcinoma. Finally, the regimen of immunosuppression or the renal transplantation in connection with which it is given, or both, appears to increase the risk from several types of cancer, most notably reticulum cell sarcoma and liver cell carcinoma.

The most difficult category to deal with consists of commonly used drugs that have not definitively been shown to be carcinogenic for man, but about which the question has been seriously raised. It has been suggested that diphenylhydantoin (Dilantin®) produces lymphoma, that amphetamines are related to Hodgkin's disease and that rauwolfia preparations produce breast cancer. In each instance, subsequent studies have failed to reproduce the original findings, and it seems unlikely that these effects, if real, are sizable. Case studies have linked chloramphenicol and other bone marrow depressants to the development of leukemia and the hypothesis is credible, but there is no epidemiological evidence in support of it.

Somewhat more credible evidence is available in support of the carcinogenicity of other preparations. Coal tar and creosote preparations may well cause skin cancer on sites of repeated application. Oral contraceptives have been studied extensively, and clearly do not increase the risk of breast cancer over the short term. Whether this will be true over the long term, particularly in young women who have many years of exposure, cannot yet be established. However, some oral contraceptive agents do seem to produce a small but real excess risk of liver adenoma, dangerous because of the tendency of the lesions to bleed. There is also some inconclusive evidence that endometrial cancer in younger women may be related to sequential contraceptive preparations.

At the head of the list must appear exogenous estrogens as used in the treatment of menopausal symptoms. Among the most widely dispensed of agents, estrogens have long been suspected of some carcinogenic action in man, but their full impact is only now becoming apparent. Several studies have indicated greater than a five-fold increase in the risk of endometrial cancer in estrogen users, and an apparent recent increase in the trend in incidence may reflect the wide use of these preparations. While the question of the carcinogenicity of estrogens for the breast is not yet resolved, it seems very unlikely that any effect of remotely comparable magnitude exists.

THOMAS M. MACK, MD

REFERENCES

Hoover R: Drugs, *In* Fraumeni JF Jr (Ed): In Persons at Risk of Cancer—An Approach to Cancer Etiology and Control. New York, Academic Press, Inc, 1975, pp 185-199

Mack TM, Pike MC, Henderson BE, et al: Estrogens and endometrial cancer in a retirement community. N Engl J Med (In Press)

Better Recognition of Minor Venereal Diseases

THE REPORTABLE venereal diseases are gonorrhea, syphilis, lymphogranuloma venereum, chancroid and granuloma inguinale. Little emphasis in recent years has been placed on the diagnosis and treatment of the latter three, and, therefore, few cases have been reported.

The diagnosis of lymphogranuloma venereum should be based on both clinical findings and laboratory confirmation. The clinical course involves an incubation period of 3 to 21 days (usually 7 to 12 days). The lesion then appears as an evanescent, painless vesicle or papule at the site of contact, followed in 1 to 30 days by regional lymphadenitis in nodes draining the inoculation site. Dissemination via the lymphatics occurs. Progression of the disease may produce chronic buboes, elephantiasis, fistulae, strictures and esthiomene.

There is no good screening test for lymphogranuloma venereum. The Frei skin test usually does not become positive until 12 to 40 days after the appearance of the primary lesion. It usually remains positive for life and approaches a 70 percent sensitivity. The complement fixation test (LGV-CFT) is 90 to 95 percent sensitive and usually becomes positive one to three weeks after infection. Both of the above tests aid in

confirming the clinical impression. Immunofluorescence and neutralization tests more specific for lymphogranuloma venereum are currently being evaluated as diagnostic tools.

The current treatment of choice is with tetracycline. Sulfisoxazole may also be used. Therapy should be continued until a cure is achieved.

Chancroid has an incubation period of two to five days followed by a shallow, painful, soft, dirty ulcer at the point of contact. Multiple lesions are common, regional lymphadenitis occurs, and extragenital occurrence of the disease may be seen.

Diagnosis most commonly is made when the clinical presentation is consistent with chancroid and any one of the following features: (1) rugged serpiginous ulceration of the coronal sulcus; (2) severely erosive lesions, and (3) a classical unilateral bubo. Culture of the organism is often difficult. Gram staining or the use of Barritt's modification of Pappenheim's pyronin methyl green stain may be used on smears of ulcers or bubo aspirates with identification of organisms resembling Hemophilus ducreyi (diagnosis is presumptive). Fluorescent antibody staining, if available, is specific and sensitive. The ducreyi skin test antigen is no longer available.

The current treatment of choice is with sulfisoxazole. Tetracycline may also be used. Administration of both should be continued until effective cure is achieved. Streptomycin and kanomycin are reserved for resistant and erosive lesions. Buboes should be aspirated as incision and drainage is contraindicated.

Granuloma inguinale has a unknown incubation period with the estimate being 8 to 80 days. The clinical course is characterized by the insidious onset of a usually painless papule or nodule. This lesion erodes leaving a beefy red granular base. Lymphadenopathy may be present.

The diagnosis may be made by scraping the base of a lesion and identifying Donovan bodies using a Wright or Giemsa stain of the material. Tissue biopsy may also be done for identification.

The current treatment of choice is with either tetracycline or streptomycin. Administration of the medication should be continued until a cure has been effected.

STEPHAN BILLSTEIN, MD

REFERENCES

Hart G: Chancroid, donovanosis, lymphogranuloma venereum. Atlanta, DHEW Publication No. (CDC) 75-8302, 1975

Tavs LE: Chancroid, lymphogranuloma venereum, granuloma inquinale, chapters 51, 52, 53, *In* Hoeprich PD (Ed): Infectious Diseases. Hagerstown, MD, Harper and Row, 1972, pp 557-571

The Use of the FTA-ABS Test for Syphilis

THE FLUORESCENT TREPONEMAL ANTIBODY-ABSORBED (FTA-ABS) test is the most highly specific and sensitive test for syphilis and has generally replaced the TPI (Treponema pallidum immobilization) test. Its chief use is to confirm reactive reagin or screening tests for syphilis—such as the Venereal Disease Research Laboratories (VDRL) or rapid plasma reagin (RPR)—in order to distinguish between syphilis cases and "false positive" reactions. It is also useful in the diagnosis of late syphilis when the reagin tests may have become negative. Once positive it generally remains reactive for life, despite therapy, and therefore cannot be utilized to evaluate treatment. It is not appropriately used as a screening test for syphilis because of technical difficulties in making tests on a large number of specimens. The significance of a reactive FTA test on spinal fluid, when the VDRL is negative, has not been established.

The FTA-ABS test is generally reported to physicians as "negative," "borderline" or "reactive." Negative indicates no treponemal antibody present and occurs in incubating or early primary syphilis as well as in uninfected persons. Borderline test results are simply inconclusive and tests should be repeated. If results of a second test are still borderline and clinical data do not indicate syphilis, the patient should be considered not infected. Reactive FTA-ABS tests indicate presence of treponemal antibody, usually a syphilis infection, but in a small percentage of people a positive FTA-ABS may occur in the absence of treponemal disease. This situation most often is found in the presence of abnormal globulins in the blood.

The FTA-ABS is not a quantitative test, but in the laboratory the degree of fluorescence observed when the test is read is recorded as 1+, 2+, 3+ or 4+. The amount of fluorescence may vary on repetition of the test with the same sample of blood or on subsequent samples from the same person; therefore many laboratories do not report the degree of fluorescence for fear of confusing the physician. In general, however, a weakly fluorescent specimen is more likely to be a false positive than a strongly fluorescing one. When clinical features are not suggestive of syphilis in a patient whose FTA-ABS test has been reported as reactive, the laboratory should be asked to provide information on the degree of fluorescence